PATENT

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#9

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Gilchrist, Tom et al.

Serial No : 09/763,983 Examiner : Wells,Lauren Q.

Filed : February, 28 2001 Art Unit : 1617

For : FOAMABLE FORMULATION AND FOAM

DECLARATION UNDER 37 CFR § 1.132 of EDITH TRAINER

Box Fee Amendment
Commissioner for Patents
Washington, D.C. 20231

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CERTIFICATE OF MAILING
UNDER 37 C.F.R. 1.8(a)

I hereby certify that this paper, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date indicated below, with sufficient postage, as first class mail, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.

BY Lori Aichele

DATE: December 31, 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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For : Foamable Formulation and Foam

DECLARATION UNDER 37 CFR § 1.132 of Eilidh TRAINER

I, Eilidh Trainer (née Gilchrist), a British citizen of 6 Greenfield Avenue, Alloway, Ayr, KA7 4NW, United Kingdom, do hereby declare as follows:

1. I am employed by Giltech Limited, 9/12 North Harbour Estate, Ayr, Scotland KA8 8BN, United Kingdom as a manager of finance and administration and as a project manager. One of my particular duties is the development and reduction to practice of various foams intended to be used for medical treatment.

2. I am a co-inventor of US Application Serial No. 09/763,983, the Application in suit.

3. I have read and understood the Office Action dated June 2, 2002 issued for US Application Serial No 09/763,983. The Examiner considers that this Application lacks novelty over International Patent No. WO96/17595 (Glichrist et al.). I am the sole inventor of WO96/17595.

4. At page 6, lines 5 to 7 of WO96/17595 it is stated, with respect to a gel formulation that:

> "It is also possible, however, to sterilise the formulation by other means, for example by γ-irradiation or e-beam radiation."

5. Upon investigation, I uncovered that carrying out sterilisation by gamma-irradiation or ethylene oxide on

the foams (as opposed to the gel formulations) described in WO96/17595 had deleterious effect on the foam structure and its capacity to absorb saline solution and that the foams often reverted to gels.

6. This finding is demonstrated by an experiment (Experiment 1) that I personally carried out. Experiment 1 shows the effect of sterilisation (using γ-irradiation or ethylene oxide (ETO)) on the capacity of foams described in the prior art and not made according to the method of Claim 1 of the Application in suit, to absorb saline solution and on their structures. Three pre-foamed formulations were made in the laboratory. These formulations were made by mixing 0g, 2.5g or 5g of calcium citrate per 100g of gel code 5. The foam samples were left to cure and dry and were cut into 5 x 5 cm squares. Four foam samples from each batch were packaged. The samples exposed to ETO sterilisation were placed in ETO sterilisable paper pouches, the samples exposed to γ-irradiation were placed in γ-sterilisable foil pouches. The samples were placed into the pouches and the pouches were heat sealed. One foam sample from each batch was retained as control; a foam sample for each batch was submitted to ETO sterilisation at cycle 5mg/l; a foam sample from each batch was submitted to ETO sterilisation at cycle 33mg/l; and a foam sample from each batch was submitted to γ-irradiation at 32Kgy. On return from sterilisation, all three foam samples which had been submitted to γ-irradiation had degraded and reverted back to gels. The non-calcium citrate containing foam sample had reverted back to a thin gel, the 2.5g calcium citrate containing foam sample had degraded to a thick gel and the 5g calcium citrate containing foam sample had degraded to a thick gel with small dense bubbles. None of these samples were able to be removed from the packaging for absorption trials and were therefore disregarded. The remaining seven foam samples which had been subjected to ETO sterilisation were put into petri dishes. The weight

of the dry foam samples were noted. The same volume of a saline solution prepared in the laboratory at a concentration of 0.9% w/v was added to each of the foam samples. At varying time intervals the samples were removed from the petri dishes and weighed. Additional saline was added to each of the samples after four hours. The resulting data is shown in Table 1. Both of the non-calcium citrate containing samples exposed to ethylene oxide reverted to a thick gel but the calcium citrate containing samples were still foams although darker in colour, thinner and more dense.

7. I conclude from Experiment 1 that γ-irradiation and ethylene oxide sterilisation both have a detrimental effect on the foams. The effect would appear to be less destructive in samples with a higher calcium content. Ethylene oxide sterilisation has a less detrimental effect on foam than gamma sterilisation.

8. In order to demonstrate that a foam obtained using a method encompassed by Claim 1 of the Application in suit is more resistant than the ones previously known, I have carried out a comparative experiment (Experiment 2). Experiment 2 shows the absorption characteristics of a saline solution of 1) foams which have been treated with precipitant prior to sterilisation using γ-irradiation or ethylene oxide (ETO) compared to 2) foams of the prior art (as described in WO 96/17595) which have not been treated with a precipitant.

9. Experiment 2 was carried out as follows:
two pre-foamed formulations were made in the laboratory. These formulations were made by mixing either 2.5g or 5g of calcium citrate per 100g of gel code 5. The foam samples were left to cure and dry and were each cut into 6 squares of 5 x 5 cm. Half of the foam samples for each of the two foam formulas were washed in a calcium chloride solution bath and left to dry. The bath was made by weighing 5gm of calcium chloride into a beaker

and forming a 100gm solution by adding distilled water. Three foam samples from each batch of washed and non-washed foams were packaged, one for ETO sterilisation at cycle 5mg/l, one for ETO sterilisation at cycle 33mg/l and one for sterilisation by γ-irridiation at 32Kgy. The 12 foam samples were put into petri dishes. The weight of the dry foam samples were noted. An identical volume of saline solution in the laboratory at a concentration of 0.9% w/v was added to each of the samples. At varying time intervals the samples were removed from the petri dishes and weighed. Additional saline was added to each of the samples after four hours. The resulting data is shown in Table 2. On return from sterilisation it was observed that all the foam samples were still in the form of foam but had darkened in colour. In removing the samples for saline absorption testing it was observed that the gamma sterilised foam samples were more dense and moist that the samples exposed to ethylene oxide. The samples sterilised by γ-irradiation, which had not been washed in calcium ion solution prior to irradiation reverted back to a gel once bathed in saline. The samples that were washed in calcium ion solution performed better after sterilisation by either gamma or ETO although the samples produced with the higher calcium content (i.e. 5g calcium citrate per 100g gel) were superior. The higher the calcium content however the less pliable the foam appeared to be.

10. Based on my observations I believe the foams described in WO96/17595 cannot be sterilised using gamma-irradiation whilst maintaining their structure integrity and that the use of ETO to sterilise such foams will result in degraded absorbtion capacity and therefore a decrease in the quality of the foam.

11. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the

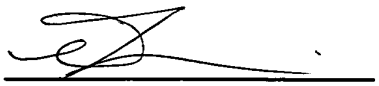
knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such wilful false statements may jeopardise the validity of the Application in suit or any Patent issuing thereon.

Date : 20th December 2002 Signed : _____

Eilidh Trainer

Experiment 1 - Table 1

This is table 1 mentioned in my Declaration under 37 CFR § 1.132 in relation to US Patent Application No 09/763,983



20th December 2002

Eilidh TRAINER **Date**

Sterilised by Ethylene Oxide	Amt. Of Calc Citrate/g in 100g gel.	Dry Weight	End Weight Gain	Saline Added	Top-up Saline At 4 hrs	Weight/g Taken at Time Intervals			
						2 hours	4 hours	6 hours	8 hours
N	0	4.48	N/A	15g	10g	Gel	Gel	Gel	Gel
N	2.5	3.02	19.87	15g	10g	16.65	19.38	22.41	22.89
N	5	3.97	19.15	15g	10g	17.03	20.23	23.06	23.12
Y	2.5	4.31	14.40	15g	10g	11.12	14.55	18.22	18.71
Y	5	3.34	16.98	15g	10g	15.54	16.28	20.14	20.32
Y	2.5	4.22	14.75	15g	10g	12.02	15.97	18.12	18.97
Y	5	4.41	16.95	15g	10g	14.34	16.81	20.77	21.36

TABLE 1

Experiment 2 - Table 2

This is table 2 mentioned in my Declaration under 37 CFR § 1.132 in relation to US Patent Application No 09/763,983

Eilidh TRAINER

20th December 2002

Date

Washed in Calcium ion Precipitation Bath	Sterilised by γ-irradiation	Sterilised by Ethylene Oxide	No. g Calcium Citrate	Dry Weight	End Weight Gain	Saline Added	Top-up Saline 4 hrs	Weight/g Taken at Time Intervals			
								2 hours	4 hours	6 hours	8 hours
N	Y	N	2.5	4.02	N/A	15g	10g	gel	gel	gel	gel
N	N	Y	2.5	4.25	14.01	15g	10g	14.75	16.12	17.27	18.26
N	N	Y	2.5	3.85	14.18	15g	10g	12.51	15.07	17.03	18.03
N	Y	N	5.0	4.63	N/A	15g	10g	gel	gel	gel	gel
N	N	Y	5.0	3.78	15.96	15g	10g	14.46	17.28	18.20	19.74
N	N	Y	5.0	4.44	15.57	15g	10g	15.77	18.53	19.39	20.01
Y	Y	N	2.5	4.87	7.34	15g	10g	7.10	10.18	11.75	12.21
Y	N	Y	2.5	4.22	12.34	15g	10g	12.75	13.77	14.86	16.56
Y	N	Y	2.5	4.51	12.18	15g	10g	13.33	14.35	15.22	16.69
Y	Y	N	5.0	3.43	8.90	15g	10g	6.32	8.88	11.96	12.33
Y	N	Y	5.0	3.95	13.73	15g	10g	12.57	14.71	15.88	17.68
Y	N	Y	5.0	3.84	14.00	15g	10g	12.13	13.65	15.99	17.84

TABLE 2